

10/686884

FILE 'REGISTRY' ENTERED AT 10:38:11 ON 08 JUN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 7 JUN 2007 HIGHEST RN 936802-99-2
DICTIONARY FILE UPDATES: 7 JUN 2007 HIGHEST RN 936802-99-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

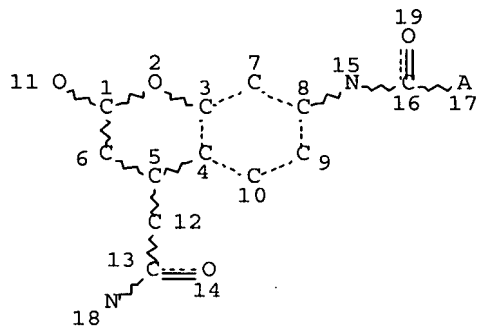
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

L1 STR



NODE ATTRIBUTES:

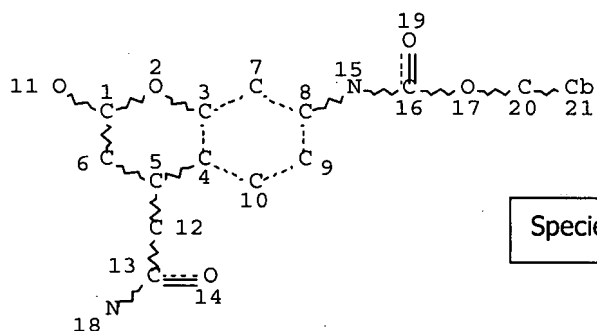
NSPEC IS RC AT 17
CONNECT IS X2 RC AT 6
CONNECT IS X2 RC AT 7
CONNECT IS X2 RC AT 9
CONNECT IS X2 RC AT 10
CONNECT IS X2 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 116 SEA FILE=REGISTRY SSS FUL L1
L3 STR



Species wherein R15 = amine protecting group = FMOC (Claim 86)

NODE ATTRIBUTES:

CONNECT IS X2 RC AT 6
 CONNECT IS X2 RC AT 7
 CONNECT IS X2 RC AT 9
 CONNECT IS X2 RC AT 10
 CONNECT IS X2 RC AT 12
 DEFAULT MLEVEL IS ATOM
 GGCAT IS PCY AT 21
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L4 1 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

100.0% PROCESSED 1 ITERATIONS
 SEARCH TIME: 00.00.01

1 ANSWERS

FILE 'CAPLUS' ENTERED AT 10:45:21 ON 08 JUN 2007
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

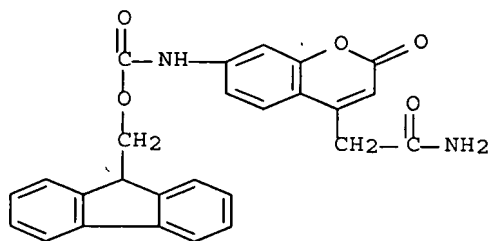
FILE COVERS 1907 - 8 Jun 2007 VOL 146 ISS 25
 FILE LAST UPDATED: 7 Jun 2007 (20070607/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

L5 1 L4

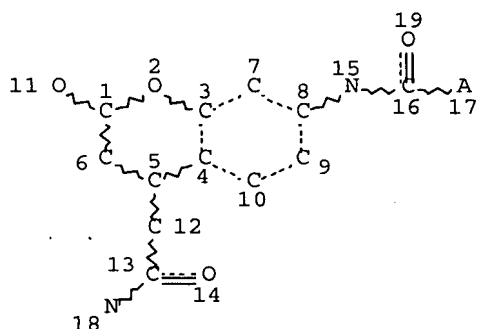
L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:34208 CAPLUS Full-text
DOCUMENT NUMBER: 136:232179
TITLE: Expedient Solid-Phase Synthesis of Fluorogenic
Protease Substrates Using the 7-Amino-4-
carbamoylethylcoumarin (ACC) Fluorophore
AUTHOR(S): Maly, Dustin J.; Leonetti, Francesco; Backes,
Bradley J.; Dauber, Deborah S.; Harris, Jennifer
L.; Craik, Charles S.; Ellman, Jonathan A.
CORPORATE SOURCE: Department of Chemistry, University of California,
Berkeley, CA, 94720, USA
SOURCE: Journal of Organic Chemistry (2002), 67(3),
910-915
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:232179
AB A highly efficient solid-phase synthesis method for the preparation of
fluorogenic protease substrates based upon the bifunctional leaving group 7-
amino-4-carbamoylethylcoumarin (ACC) is reported. Methods for the large-
scale preparation of the novel fluorogenic leaving-group ACC are provided.
Detailed procedures are also provided for loading a diverse set of amino acids
to support-bound ACC in good yields and with minimal racemization. Finally,
procedures are included for the preparative synthesis of optimized ACC
substrates for HIV-1 protease and plasmin.
IT 403518-84-3DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(solid-phase preparation of amino(carbamoylethyl)coumarin derivs. of
amino acids and peptides as fluorogenic substrates for proteases)
RN 403518-84-3 CAPLUS
CN Carbamic acid, [4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]-,
9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27. THERE ARE 27 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

(FILE 'REGISTRY' ENTERED AT 10:36:47 ON 08 JUN 2007)

L1 STR



Str. Claim 84

NODE ATTRIBUTES:

NSPEC IS RC AT 17
 CONNECT IS X2 RC AT 6
 CONNECT IS X2 RC AT 7
 CONNECT IS X2 RC AT 9
 CONNECT IS X2 RC AT 10
 CONNECT IS X2 RC AT 12
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 116 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 366 ITERATIONS
 SEARCH TIME: 00.00.01

116 ANSWERS

FILE 'CAPLUS' ENTERED AT 10:46:29 ON 08 JUN 2007

L6 15 S L2
 L7 14 S L6 NOT L5

E1 THROUGH E86 ASSIGNED

L7 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 24 Aug 2006

ACCESSION NUMBER: 2006:847205 CAPLUS Full-text

DOCUMENT NUMBER: 145:438883

TITLE: Hydrophilic photolabeling of glycopeptides from
 the murine liver-intestine (LI) cadherin
 recognition domain

AUTHOR(S): Heiner, Sebastian; Detert, Heiner; Kuhn, Axel;
 Kunz, Horst

CORPORATE SOURCE: Institut fuer Organische Chemie, Universitaet
 Mainz, Mainz, D-55099, Germany

SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(18),
 6149-6164

CODEN: BMECEP; ISSN: 0968-0896

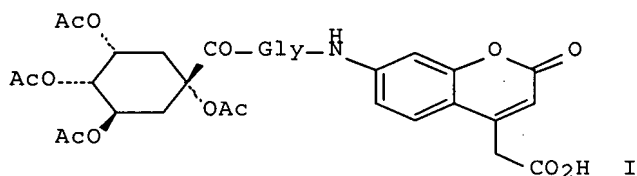
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:438883

GI



AB LI-Cadherin is a transmembrane glycoprotein involved in cell adhesion of epithelial cells. Its supposed recognition domain contains the peptide motif AAL and is distinctly hydrophobic. In order to obtain sufficiently soluble model compds., glycan side chains of T-antigen, (2,6)sialyl T-antigen and sialyl TN-antigen structure were linked to the serine located in the supposed turn sequence of the LI-cadherin recognition domain. A quinic acid-glycine-7-amino-coumarin I (Quiglac) chromophore was constructed in order to enhance the solubility of labeled LI-cadherin glycopeptides in water.

IT 912840-53-0P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(UV absorption spectra; solid-phase preparation of hydrophilic, photolabeled glycopeptides from LI cadherin recognition domain)

IT 912840-50-7P 912840-52-9P 912840-63-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(solid-phase preparation of hydrophilic, photolabeled glycopeptides from LI cadherin recognition domain)

IT 912840-65-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase preparation of hydrophilic, photolabeled glycopeptides from LI cadherin recognition domain)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L7 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 01 May 2006

ACCESSION NUMBER: 2006:396768 CAPLUS Full-text

DOCUMENT NUMBER: 145:42081

TITLE: Substrate Profiling of Cysteine Proteases Using a
Combinatorial Peptide Library Identifies
Functionally Unique Specificities

AUTHOR(S): Choe, Youngchool; Leonetti, Francesco; Greenbaum,
Doron C.; Lecaille, Fabien; Bogyo, Matthew;
Broemme, Dieter; Ellman, Jonathan A.; Craik,
Charles S.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University
of California at San Francisco, CA, 94143, USA

SOURCE: Journal of Biological Chemistry (2006), 281(18),
12824-12832

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The substrate specificities of papain-like cysteine proteases (clan CA, family C1) papain, bromelain, and human cathepsins L, V, K, S, F, B, and five

proteases of parasitic origin were studied using a completely diversified positional scanning synthetic combinatorial library. A bifunctional coumarin fluorophore was used that facilitated synthesis of the library and individual peptide substrates. The library has a total of 160,000 tetrapeptide substrate sequences completely randomizing each of the P1, P2, P3, and P4 positions with 20 amino acids. A microtiter plate assay format permitted a rapid determination of the specificity profile of each enzyme. Individual peptide substrates were then synthesized and tested for a quant. determination of the specificity of the human cathepsins. Despite the conserved three-dimensional structure and similar substrate specificity of the enzymes studied, distinct amino acid preferences that differentiate each enzyme were identified. The specificities of cathepsins K and S partially match the cleavage site sequences in their physiol. substrates. Capitalizing on its unique preference for proline and glycine at the P2 and P3 positions, resp., selective substrates and a substrate-based inhibitor were developed for cathepsin K. A cluster anal. of the proteases based on the complete specificity profile provided a functional characterization distinct from standard sequence anal. This approach provides useful information for developing selective chemical probes to study protease-related pathologies and physiologies.

IT 890405-98-8 890405-99-9 890406-00-5
890406-01-6 890406-02-7 890406-03-8
890406-04-9 890406-05-0 890406-06-1

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(substrate; substrate profiling of cysteine proteinases using
combinatorial peptide library identifies functionally unique
specificities)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L7 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 03 Mar 2006

ACCESSION NUMBER: 2006:197317 CAPLUS Full-text

DOCUMENT NUMBER: 144:406993

TITLE: Determination of the Substrate Specificity of
Tripeptidyl-peptidase I Using Combinatorial
Peptide Libraries and Development of Improved
Fluorogenic Substrates

AUTHOR(S): Tian, Yu; Sohar, Istvan; Taylor, John W.; Lobel,
Peter

CORPORATE SOURCE: Center for Advanced Biotechnology and Medicine,
the State University of New Jersey, Piscataway,
NJ, 08854, USA

SOURCE: Journal of Biological Chemistry (2006), 281(10),
6559-6572

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Classical late-infantile neuronal ceroid lipofuscinosis is a fatal
neurodegenerative disease caused by mutations in CLN2, the gene encoding the
lysosomal protease tripeptidyl-peptidase I (TPP I). The natural substrates
for TPP I and the pathophysiol. processes associated with lysosomal storage
and disease progression are not well understood. Detailed characterization of
TPP I substrate specificity should provide insights into these issues and also
aid in the development of improved clin. and biochem. assays. To this end, we
constructed fluorogenic and standard combinatorial peptide libraries and
analyzed them using fluorescence and mass spectrometry-based activity assays.

The fluorogenic group 7-amino-4-carbamoylmethylcoumarin was incorporated into a series of 7-amino-4-carbamoylmethylcoumarin tripeptide libraries using a design strategy that allowed systematic evaluation of the P1, P2, and P3 positions. TPP I digestion of these substrates liberates the fluorescence group and results in a large increase in fluorescence that can be used to calculate kinetic parameters and to derive the substrate specificity constant k_{cat}/K_M . In addition, we implemented a mass spectrometry-based assay to measure the hydrolysis of individual peptides in peptide pools and thus expand the scope of the anal. Nonfluorogenic tetrapeptide and pentapeptide libraries were synthesized and analyzed to evaluate P1' and P2' residues. Together, this anal. allowed us to predict the relative specificity of TPP I toward a wide range of potential biol. substrates. In addition, we evaluated a variety of new fluorogenic peptides with a P3 Arg residue, and we demonstrated their superiority compared with the widely used substrate Ala-Ala-Phe-AMC for selectively measuring TPP I activity in biol. specimens.

IT 884005-67-8 884005-68-9 884005-69-0
 884005-70-3 884005-71-4 884005-74-7
 884005-75-8 884005-76-9 884005-77-0
 884005-78-1 884005-79-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (determination of substrate specificity of tripeptidyl-peptidase I using
 combinatorial peptide libraries and development of improved
 fluorogenic substrates)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L7 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 26 Aug 2005

ACCESSION NUMBER: 2005:902691 CAPLUS Full-text

DOCUMENT NUMBER: 143:224928

TITLE: Designing of prostatic substrates and inhibitors
 for targeting and inhibiting prostatic activity

INVENTOR(S): Harris, Jennifer; Shipway, Aaron

PATENT ASSIGNEE(S): IRM LLC, Bermuda

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005076886	A2	20050825	WO 2005-US3363	20050204
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005222383	A1	20051006	US 2005-51494	20050204
PRIORITY APPLN. INFO.:			US 2004-542163P	P 20040205

OTHER SOURCE(S): MARPAT 143:224928

AB The invention provides substrate specificity profiles for serine protease prostatic. Optimal prostatic substrate sequences, both to the prime side and non-prime side of the prostatic recognition site, are disclosed herein. The prostatic substrate sequences are used in designing substrates, inhibitors, and prodrugs. Prostatic inhibitors based on substrate specificity are also provided. Metal ions on substrate-assisted catalysis and substrate specificity is also provided. The results indicate that the classical inhibition consts. of aprotinin, α 1-antitrypsin, α 1-antichymotrypsin, and SBTI on prostatic are 2.5nM, >10 μ M, >0.2 μ M, and >10 μ M, resp.

IT 862896-00-2

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(prostatic substrate; designing of prostatic substrates and inhibitors for targeting and inhibiting prostatic activity)

L7 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 03 Aug 2005

ACCESSION NUMBER: 2005:690452 CAPLUS Full-text

DOCUMENT NUMBER: 143:262392

TITLE: Functional Profiling of Recombinant NS3 Proteases from All Four Serotypes of Dengue Virus Using Tetrapeptide and Octapeptide Substrate Libraries

AUTHOR(S): Li, Jun; Lim, Siew Pheng; Beer, David; Patel, Viral; Wen, Daying; Tumanut, Christine; Tully, David C.; Williams, Jennifer A.; Jiricek, Jan; Priestle, John P.; Harris, Jennifer L.; Vasudevan, Subhash G.

CORPORATE SOURCE: Genomics Institute of the Novartis Research Foundation, San Diego, CA, 92121, USA

SOURCE: Journal of Biological Chemistry (2005), 280(31), 28766-28774

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Regulated proteolysis by the two-component NS2B/NS3 protease of dengue virus is essential for virus replication and the maturation of infectious virions. The functional similarity between the NS2B/NS3 proteases from the four genetically and antigenically distinct serotypes was addressed by characterizing the differences in their substrate specificity using tetrapeptide and octapeptide libraries in a positional scanning format, each containing 130,321 substrates. The proteases from different serotypes were shown to be functionally homologous based on the similarity of their substrate cleavage preferences. A strong preference for basic amino acid residues (Arg/Lys) at the P1 positions was observed, whereas the preferences for the P2-4 sites were in the order of Arg > Thr > Gln/Asn/Lys for P2, Lys > Arg > Asn for P3, and Nle > Leu > Lys > Xaa for P4. The prime site substrate specificity was for small and polar amino acids in P1' and P3'. In contrast, the P2' and P4' substrate positions showed minimal activity. The influence of the P2 and P3 amino acids on ground state binding and the P4 position for transition state stabilization was identified through single substrate kinetics with optimal and suboptimal substrate sequences. The specificities observed for dengue NS2B/NS3 have features in common with the physiologic cleavage sites in the dengue polyprotein; however, all sites reveal previously unrecognized suboptimal sequences.

IT 863975-27-3

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(substrate; positional specificity of recombinant NS3 proteinases from all four dengue virus serotypes using tetrapeptide and octapeptide substrate libraries)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 13 Mar 2005

ACCESSION NUMBER: 2005:220009 CAPLUS Full-text

DOCUMENT NUMBER: 142:293714

TITLE: Specificity and modulators of transmembrane protease serine 6 (TMPRSS6), role of TMPRSS6 in proteolytic activation of pathogenic toxins, and the use in screening for antibacterial agents

INVENTOR(S): Harris, Jennifer; Shipway, Aaron

PATENT ASSIGNEE(S): Irm Llc, Bermuda

SOURCE: U.S. Pat. Appl. Publ., 21 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005054027	A1	20050310	US 2004-933666	20040903
WO 2005023835	A2	20050317	WO 2004-US28686	20040903

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-501301P

P 20030909

AB This invention provides novel methods for identifying modulators of transmembrane protease serine 6 (TMPRSS6). The methods comprise screening test agents for ability to modulate proteolysis of a pathogenic toxin substrate or a synthetic peptide substrate of TMPRSS6. The optimal peptide substrate of TMPRSS6 was synthesized. The screening method comprises: (a) examining proteolysis of the toxin by TMPRSS6 in the presence of test agents; and (b) identifying a test agent that inhibits proteolysis of the toxin by TMPRSS6. The methods can further comprise screening the identified modulating agents for ability to inhibit infections of pathogens. Also provided in the invention are methods and pharmaceutical compns. for treating infections of pathogens whose toxins are proteolytically activated by TMPRSS6. More specifically, protease activity and substrate specificity of TMPRSS6 was studied. Inhibition of TMPRSS6 by camostat mesylate was shown. Cleavage of bacterial toxins by TMPRSS6 was studied. It was suggested that TMPRSS6 could play a role in proteolytic activation of the various pathogenic toxins under physiol. conditions. The cDNA sequence and the encoded amino acid sequence of human TMPRSS6 are also provided.

IT 847549-05-7 847549-06-8 847549-07-9

847549-08-0

RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(TMPRSS6 substrate; specificity and modulators of transmembrane protease serine 6 (TMPRSS6), role of TMPRSS6 in proteolytic activation of pathogenic toxins, and use in screening for antibacterial agents)

L7 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 21 Mar 2003

ACCESSION NUMBER: 2003:220003 CAPLUS Full-text

DOCUMENT NUMBER: 138:381255

TITLE: Enzymatic Profiling System in a Small-Molecule Microarray

AUTHOR(S): Zhu, Qing; Uttamchandani, Mahesh; Li, Dongbo; Lesaicherre, Marie L.; Yao, Shao Q.

CORPORATE SOURCE: Departments of Chemistry and Biological Sciences, National University of Singapore, Singapore, 117543, Singapore

SOURCE: Organic Letters (2003), 5(8), 1257-1260
CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:381255

AB We have developed a microarray-based strategy for detection of three major classes of hydrolytic enzymes on the basis of their catalytic activities. This enables the sensitive detection of proteins not merely by their bindings but rather by their enzymic activities. This may provide a valuable tool for screening, identification, and characterization of new enzymes in a high-throughput fashion.

IT 525578-92-1P 525578-93-2P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(enzymic profiling system in small-mol. microarray)

IT 525579-01-5P 525579-02-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enzymic profiling system in small-mol. microarray)

IT 608529-60-8P 608529-68-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(enzymic profiling system in small-mol. microarray)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 20 Mar 2003

ACCESSION NUMBER: 2003:215762 CAPLUS Full-text

DOCUMENT NUMBER: 139:85629

TITLE: Facile synthesis of 7-amino-4-carbamoylmethylcoumarin (ACC)-containing solid supports and Their corresponding fluorogenic protease substrates

AUTHOR(S): Zhu, Qing; Li, Dong B.; Uttamchandani, Mahesh; Yao, Shao Q.

CORPORATE SOURCE: Department of Chemistry, National University of Singapore, Singapore, 117543, Singapore

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003),

13(6), 1033-1036
 CODEN: BMCLE8; ISSN: 0960-894X
 Elsevier Science B.V.

PUBLISHER:
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 139:85629

AB The bifunctional fluorophore, 7-amino-4-carbamoylmethylcoumarin (ACC), without any protection groups was regioselectively attached to different solid supports functionalized with a primary amino group. The resulting resins were used to synthesize fluorogenic protease substrates with high yield and purity.

IT 553676-66-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of aminocarbamoylmethylcoumarin labeled peptide substrate of caspase-1)

IT 403518-96-7DP, resin-bound 525578-92-1DP,
 resin-bound 525579-01-5P 553676-58-7DP,
 resin-bound 553676-59-8DP, resin-bound 553676-62-3DP
 , resin-bound 553676-64-5DP, resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of resin-bound aminocarbamoylmethylcoumarin for solid-phase synthesis of fluorogenic peptides)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L7 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 22 Nov 2002

ACCESSION NUMBER: 2002:884241 CAPLUS Full-text

DOCUMENT NUMBER: 138:102696

TITLE: Peptide Microarrays for the Determination of
 Protease Substrate Specificity

AUTHOR(S): Salisbury, Cleo M.; Maly, Dustin J.; Ellman,
 Jonathan A.

CORPORATE SOURCE: Center for New Directions in Organic Synthesis
 Department of Chemistry, University of California,
 Berkeley, CA, 94720, USA

SOURCE: Journal of the American Chemical Society (2002),
 124(50), 14868-14870

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:102696

AB A method is described for the preparation of substrate microarrays that allow for the rapid determination of protease substrate specificity. Peptidyl coumarin substrates, synthesized on solid support using standard techniques, are printed onto glass slides using DNA microarraying equipment. The linkage from the peptide to the slide is formed through a chemoselective reaction, resulting in an array of uniformly displayed fluorogenic substrates. The arrays can be treated with proteases to yield substrate specificity profiles. Standard instrumentation for visualization of microarrays can be used to obtain comparisons of the specificity consts. for all of the prepared substrates. The utility of these arrays is demonstrated by the selective cleavage of preferred substrates with trypsin, thrombin, and granzyme B, and by assessing the extended substrate specificity of thrombin using a microarray of 361 different peptidyl coumarin substrates.

IT 487011-47-2 487011-48-3 487011-49-4

487011-50-7

RL: ARU (Analytical role, unclassified); BSU (Biological study,
 unclassified); ANST (Analytical study); BIOL (Biological study)

(peptide microarrays for determination of protease substrate specificity)

IT 296236-25-4P 487011-62-1P 487011-63-2P
 487011-64-3P 487011-65-4P 487011-66-5P
 487011-67-6P 487011-68-7P 487011-69-8P
 487011-70-1P 487011-71-2P 487011-72-3P
 487011-73-4P 487011-74-5P 487011-75-6P
 487011-76-7P 487011-77-8P 487011-78-9P
 487011-79-0P 487011-80-3P 487011-81-4P
 487011-82-5P 487011-83-6P 487011-84-7P
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation)

(peptide microarrays for determination of protease substrate specificity)

IT 487011-85-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

(peptide microarrays for determination of protease substrate specificity)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L7 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 31 Dec 2001

ACCESSION NUMBER: 2002:2518 CAPLUS Full-text

DOCUMENT NUMBER: 136:275221

TITLE: Substrate specificity of the human proteasome

AUTHOR(S): Harris, Jennifer L.; Alper, Phil B.; Li, Jun;
 Rechsteiner, Martin; Backes, Bradley J.

CORPORATE SOURCE: Genomics Institute of the Novartis Research
 Foundation, San Diego, CA, 92121, USA

SOURCE: Chemistry & Biology (2001), 8(12), 1131-1141
 CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Regulated proteolysis by the proteasome is crucial for a broad array of cellular processes, from control of the cell cycle to production of antigens. Results: The rules governing the N-terminal primary and extended substrate specificity of the human 20S proteasome in the presence or absence of 11S proteasome activators (REG α / β and REG γ) have been elaborated using activity-based proteomic library tools. Conclusions: The 11S proteasome activators are shown to be important for both increasing the activity of the 20S proteasome and for altering its cleavage pattern and substrate specificity. These data also establish that the extended substrate specificity is an important factor for proteasomal cleavage. The specificities observed have features in common with major histocompatibility complex (MHC) class I ligands and can be used to improve the prediction of MHC class I restricted cytotoxic T-cell responses.

IT 406682-97-1 406682-98-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(11S proteasome activators REG α / β and REG γ of
 human proteasome 20 play role both increasing activity of 20S
 proteasome and for altering cleavage pattern and substrate
 specificity)

IT 406682-92-6 406682-93-7 406682-94-8

406682-95-9 406682-96-0

RL: BSU (Biological study, unclassified); CST (Combinatorial study,
 unclassified); BIOL (Biological study); CMBI (Combinatorial study)

(11S proteasome activators REG α / β and REG γ of
 human proteasome 20 play role both increasing activity of 20S
 proteasome and for altering cleavage pattern and substrate

specificity)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 14 Dec 2001

ACCESSION NUMBER: 2001:904143 CAPLUS Full-text

DOCUMENT NUMBER: 136:20255

TITLE: Profiling of protease specificity using combinatorial fluorogenic substrate libraries

INVENTOR(S): Harris, Jennifer L.; Backes, Bradley J.; Ellman, Jonathan A.; Craik, Charles S.

PATENT ASSIGNEE(S): Regents of the University of California, USA

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

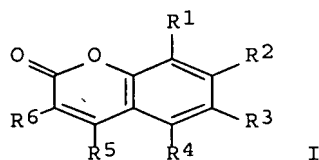
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094332	A1	20011213	WO 2001-US17265	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002022243	A1	20020221	US 2001-866132	20010525
US 6680178	B2	20040120		
US 2004175777	A1	20040909	US 2003-686884	20031015
PRIORITY APPLN. INFO.:			US 2000-209274P	P 20000602
			US 2001-866132	A 20010525
			WO 2001-US17265	A 20010525

OTHER SOURCE(S): MARPAT 136:20255
GI



AB Fluorogenic peptide substrates allow for the configuration of general substrate libraries to rapidly identify the primary and extended specificity of enzymes, such as proteases. Coumarin derivs. I [R1-R6 are H, halo, NO₂, CN, C(O)mR7, C(O)NR8R9, S(O)tR10, SO₂NR11R12, OR13, (un)substituted alkyl, -R14-SS or NHR15, where R7-R13 are H, (un)substituted alkyl or aryl; R14 is a linking group adjoining the fluorogenic moiety and the solid support (SS); R15 is an amine-protecting group, -C(O)-AA or -C(O)-P, where P is a peptide sequence and AA is an amino acid residue; m = 1 or 2; t = 0-2, with the proviso that at least one of R1-R6 is -R14-SS and at least one of R1-R6 is NHR15] are claimed. The substrates contain a fluorogenic-leaving group, such as 7-amino-4-carbamoylmethylcoumarin (ACC). Substrates incorporating the ACC leaving group show comparable kinetic profiles as those with the traditionally used 7-amino-4-methylcoumarin (AMC) leaving group. The bifunctional nature of ACC allows for the efficient production of single substrates and substrate libraries using solid-phase synthesis techniques. The approx. 3-fold increased quantum yield of ACC over AMC permits reduction in enzyme and substrate concns., so that a greater number of substrates can be tolerated in a single assay, thus enabling an increase in the diversity space of the library. Employing this screening method, the substrate specificities of a diverse array of proteases were profiled, including serine proteases and cysteine proteases.

IT 296236-25-4P 296236-27-6P 371979-74-7P
371979-75-8P 371979-76-9P 371979-77-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(profiling of protease specificity using combinatorial fluorogenic substrate libraries)

IT 378247-76-8

RL: PRP (Properties)

(profiling of protease specificity using combinatorial fluorogenic substrate libraries)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 23 Sep 2001

ACCESSION NUMBER: 2001:694697 CAPLUS Full-text

DOCUMENT NUMBER: 135:354576

TITLE: Definition of the extended substrate specificity determinants for β -tryptases I and II

AUTHOR(S): Harris, Jennifer L.; Niles, Andrew; Burdick, Keith; Maffitt, Mark; Backes, Bradley J.; Ellman, Jonathan A.; Kuntz, Irwin; Haak-Frendscho, Mary; Craik, Charles S.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Program in Chemistry and Chemical Biology, University of California San Francisco, San Francisco, CA, 94143, USA

SOURCE: Journal of Biological Chemistry (2001), 276(37), 34941-34947

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tryptases β I and β II were heterologously expressed and purified in yeast to functionally characterize the substrate specificity of each enzyme. Three positional scanning combinatorial tetrapeptide substrate libraries were used

to determine the primary and extended substrate specificity of the proteases. Both enzymes have a strict primary preference for cleavage after the basic amino acids, lysine and arginine, with only a slight preference for lysine over arginine. β I and β II tryptase share similar extended substrate specificity, with preference for proline at P4, preference for arginine or lysine at P3, and P2 showing a slight preference for asparagine. Measurement of kinetic consts. with multiple substrates designed for β -tryptases reveal that selectivity is highly dependent on ground state substrate binding. Coupled with the functional determinants, structural determinants of tryptase substrate specificity were identified. Mol. docking of the preferred substrate sequence to the three-dimensional tetrameric tryptase structure reveals a novel extended substrate binding mode that involves interactions from two adjacent protomers, including P4 Thr-96', P3 Asp-60B' and Glu-217, and P1 Asp-189. Based on the determined substrate information, a mechanism-based tetrapeptide-chloromethylketone inhibitor was designed and shown to be a potent tryptase inhibitor. Finally, the cleavage sites of several physiol. relevant substrates of β -tryptases show consistency with the specificity data presented here.

IT 371979-74-7 371979-75-8 371979-76-9
371979-77-0

RL: BPR (Biological process); BSU (Biological study, unclassified);
BIOL (Biological study); PROC (Process)
(synthetic substrate; definition of extended substrate specificity
determinants for human β -tryptases I and II)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L7 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 23 Jul 2000

ACCESSION NUMBER: 2000:494458 CAPLUS Full-text

DOCUMENT NUMBER: 133:248800

TITLE: Rapid and general profiling of protease
specificity by using combinatorial fluorogenic
substrate libraries

AUTHOR(S): Harris, Jennifer L.; Backes, Bradley J.; Leonetti,
Francesco; Mahrus, Sami; Ellman, Jonathan A.;
Craik, Charles S.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Program in
Chemistry and Chemical Biology, University of
California, San Francisco, CA, 94143, USA

SOURCE: Proceedings of the National Academy of Sciences of
the United States of America (2000), 97(14),
7754-7759

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method is presented for the preparation and use of fluorogenic peptide substrates that allows for the configuration of general substrate libraries to rapidly identify the primary and extended specificity of proteases. The substrates contain the fluorogenic leaving group 7-amino-4-carbamoylmethylcoumarin (ACC). Substrates incorporating the ACC leaving group show kinetic profiles comparable to those with the traditionally used 7-amino-4-methylcoumarin (AMC) leaving group. The bifunctional nature of ACC allows for the efficient production of single substrates and substrate libraries by using 9-fluorenylmethoxycarbonyl (Fmoc)-based solid-phase synthesis techniques. The approx. 3-fold-increased quantum yield of ACC over AMC permits reduction in enzyme and substrate concns. As a consequence, a greater

number of substrates can be tolerated in a single assay, thus enabling an increase in the diversity space of the library. Soluble positional protease substrate libraries of 137,180 and 6859 members, possessing amino acid diversity at the P4-P3-P2-P1 and P4-P3-P2 positions, resp., were constructed. Employing this screening method, we profiled the substrate specificities of a diverse array of proteases, including the serine proteases thrombin, plasmin, factor Xa, urokinase-type plasminogen activator, tissue plasminogen activator, granzyme B, trypsin, chymotrypsin, human neutrophil elastase, and the cysteine proteases papain and cruzain. The resulting profiles create a pharmacophoric portrayal of the proteases to aid in the design of selective substrates and potent inhibitors.

IT 296236-25-4P 296236-27-6P

RL: BPR (Biological process); BSU (Biological study, unclassified);
SPN (Synthetic preparation); BIOL (Biological study); PREP
(Preparation); PROC (Process)

(rapid and general profiling of protease specificity by using
combinatorial fluorogenic substrate libraries)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L7 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 26 Jul 1992

ACCESSION NUMBER: 1992:426258 CAPLUS Full-text

DOCUMENT NUMBER: 117:26258

TITLE: Synthesis and fluorescent properties of new
heterobifunctional fluorescent probes

AUTHOR(S): Besson, Thierry; Joseph, Benoit; Moreau, Pascale;
Viaud, Marie Claude; Coudert, Gerard; Guillaumet,
Gerald

CORPORATE SOURCE: Lab. Chim. Bioorg. Anal., Univ. Orleans, Orleans,
45067, Fr.

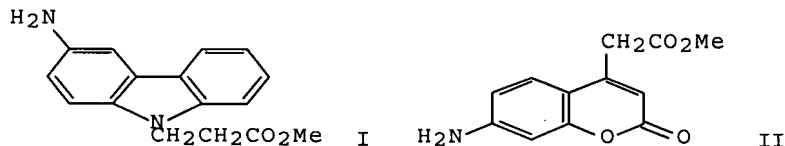
SOURCE: Heterocycles (1992), 34(2), 273-91

CODEN: HTCYAM; ISSN: 0385-5414

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Two families of heterobifunctional fluorescent mols., including I and II, derived from carbazole and coumarin possessing the same fluorescent properties as their monofunctional parent compds. were synthesized and their spectral properties investigated. The presence of the two different functional groups on these probes do not alter their lasing properties and allow many applications in cellular biochem.

IT 141692-68-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and UV and fluorescence of)

10/686884

FILE 'REGISTRY' ENTERED AT 10:48:21 ON 08 JUN 2007

L8 86 SEA FILE=REGISTRY ABB=ON PLU=ON (296236-25-4/BI OR
296236-27-6/BI OR 371979-74-7/BI OR 371979-75-8/BI OR
371979-76-9/BI OR 371979-77-0/BI OR 525578-92-1/BI OR
525579-01-5/BI OR 141692-68-4/BI OR 378247-76-8/BI OR
403518-96-7/BI OR 406682-92-6/BI OR 406682-93-7/BI OR
406682-94-8/BI OR 406682-95-9/BI OR 406682-96-0/BI OR
406682-97-1/BI OR 406682-98-2/BI OR 487011-47-2/BI OR
487011-48-3/BI OR 487011-49-4/BI OR 487011-50-7/BI OR
487011-62-1/BI OR 487011-63-2/BI OR 487011-64-3/BI OR
487011-65-4/BI OR 487011-66-5/BI OR 487011-67-6/BI OR
487011-68-7/BI OR 487011-69-8/BI OR 487011-70-1/BI OR
487011-71-2/BI OR 487011-72-3/BI OR 487011-73-4/BI OR
487011-74-5/BI OR 487011-75-6/BI OR 487011-76-7/BI OR
487011-77-8/BI OR 487011-78-9/BI OR 487011-79-0/BI OR
487011-80-3/BI OR 487011-81-4/BI OR 487011-82-5/BI OR
487011-83-6/BI OR 487011-84-7/BI OR 487011-85-8/BI OR
525578-93-2/BI OR 525579-02-6/BI OR 553676-58-7/BI OR
553676-59-8/BI OR 553676-62-3/BI OR 553676-64-5/BI OR
553676-66-7/BI OR 608529-60-8/BI OR 608529-68-6/BI OR
847549-05-7/BI OR 847549-06-8/BI OR 847549-07-9/BI OR
847549-08-0/BI OR 862896-00-2/BI OR 863975-27-3/BI OR
884005-67-8/BI OR 884005-68-9/BI OR 884005-69-0/BI OR
884005-70-3/BI OR 884005-71-4/BI OR 884005-74-7/BI OR
884005-75-8/BI OR 884005-76-9/BI OR 884005-77-0/BI OR
884005-78-1/BI OR 884005-79-2/BI OR 890405-98-8/BI OR
890405-99-9/BI OR 890406-00-5/BI OR 890406-01-6/BI OR
890406-02-7/BI OR 890406-03-8/BI OR 890406-04-9/BI OR
890406-05-0/BI OR 890406-06-1/BI OR 912840-50-7/BI OR
912840-52-9/BI OR 912840-53-0/BI OR 912840-63-2/BI OR
912840-65-4/BI)

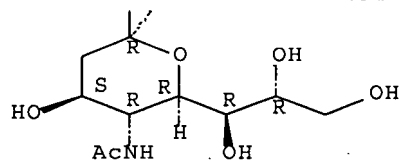
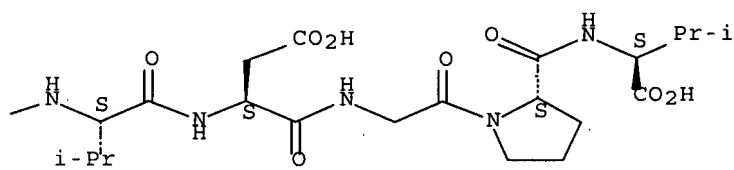
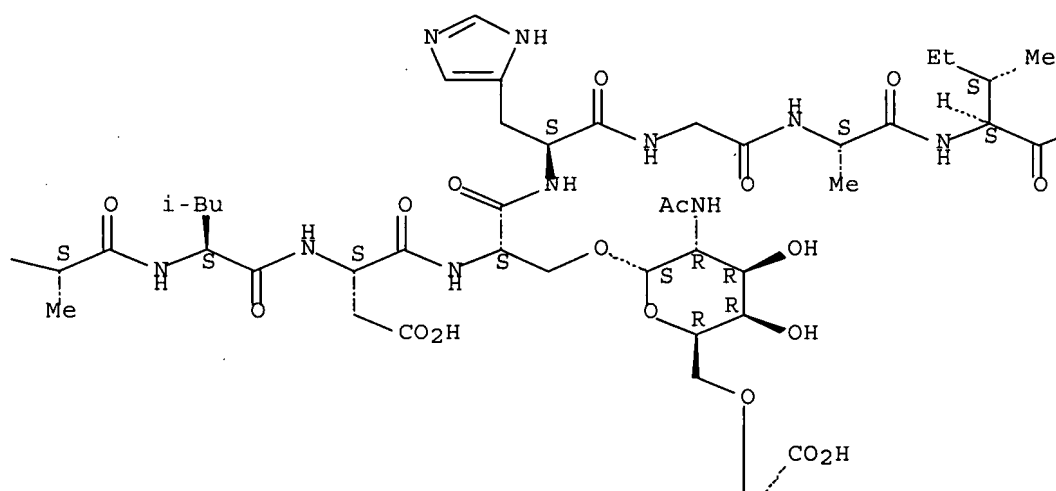
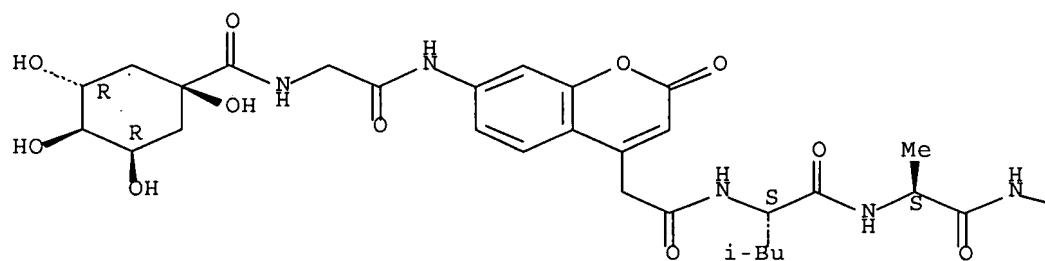
=> d 1,6,13,26-28,32,34,39,41,43,71,78-80,84,86 ide can

Random RNs/Strs displayed

L8 ANSWER 1 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 912840-65-4 REGISTRY
ED Entered STN: 09 Nov 2006
CN L-Valine, N-[[[(1 α ,3R,4 α ,5R)-1,3,4,5-
tetrahydroxycyclohexyl]carbonyl]glycyl-7-amino-2-oxo-2H-1-benzopyran-4-
acetyl-L-leucyl-L-alanyl-L-alanyl-L-leucyl-L- α -aspartyl-O-[2-
(acetylamino)-6-O-(N-acetyl- α -neuraminosyl)-2-deoxy- α -D-
galactopyranosyl]-L-seryl-L-histidylglycyl-L-alanyl-L-isoleucyl-L-
valyl-L- α -aspartylglycyl-L-prolyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C102 H153 N21 O43
SR CA
LC STN Files: CA, CAPLUS, CASREACT

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry. Rotation (-).



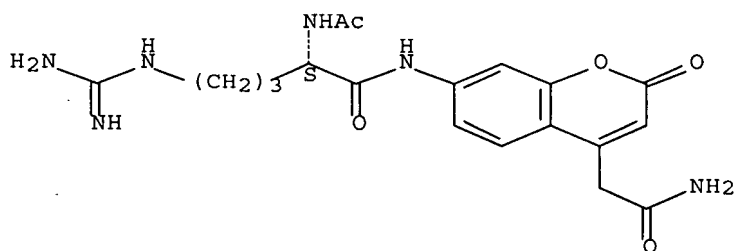
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:438883

L8 ANSWER 6 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 890406-06-1 REGISTRY
ED Entered STN: 03 Jul 2006
CN 2H-1-Benzopyran-4-acetamide, 7-[[[(2S)-2-(acetylamino)-5-
[(aminoiminomethyl)amino]-1-oxopentyl]amino]-2-oxo- (9CI) (CA INDEX
NAME)
FS STEREOSEARCH
MF C19 H24 N6 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



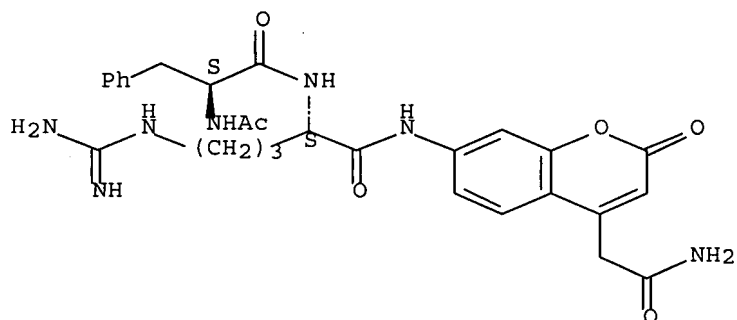
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:42081

L8 ANSWER 13 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 890405-99-9 REGISTRY
ED Entered STN: 03 Jul 2006
CN L-Argininamide, N-acetyl-L-phenylalanyl-N-[4-(2-amino-2-oxoethyl)-2-
oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H33 N7 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

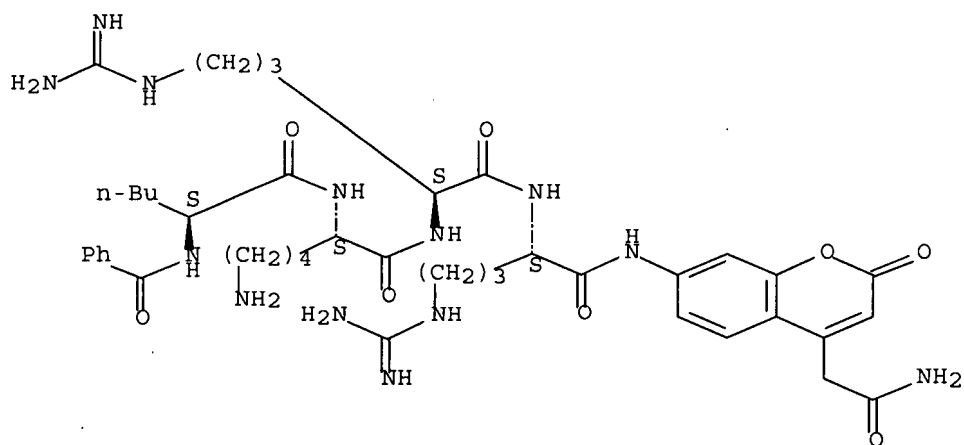
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:42081

L8 ANSWER 26 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 863975-27-3 REGISTRY
ED Entered STN: 27 Sep 2005
CN L-Argininamide, N-benzoyl-L-norleucyl-L-lysyl-L-arginyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C42 H61 N13 O8
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10/686884

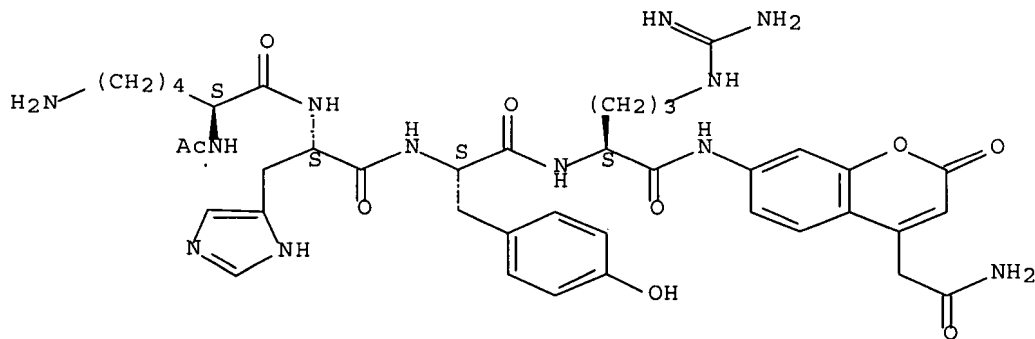
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:262392

L8 ANSWER 27 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 862896-00-2 REGISTRY
ED Entered STN: 12 Sep 2005
CN L-Argininamide, N2-acetyl-L-lysyl-L-histidyl-L-tyrosyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C40 H52 N12 O9
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP'.FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

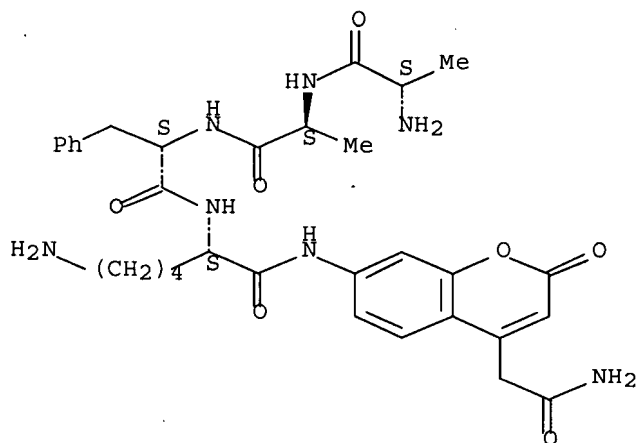
REFERENCE 1: 143:224928

L8 ANSWER 28 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 847549-08-0 REGISTRY
ED Entered STN: 30 Mar 2005
CN L-Lysinamide, L-alanyl-L-alanyl-L-phenylalanyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H41 N7 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

10/686884



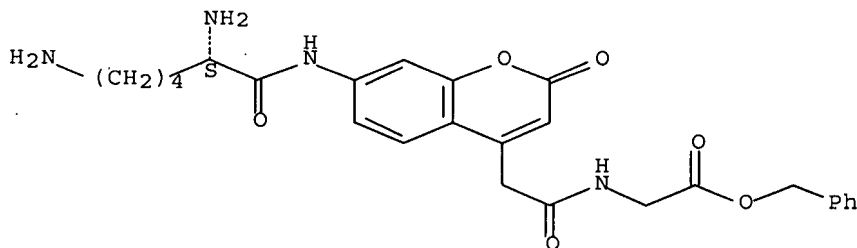
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:293714

```
L8 ANSWER 32 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 608529-68-6 REGISTRY
ED Entered STN: 24 Oct 2003
CN Glycine, L-lysyl-7-amino-2-oxo-2H-1-benzopyran-4-acetyl-, phenylmethyl
   ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H30 N4 O6
SR CA
LC STN Files: CA, CAPLUS, CASREACT
```

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:381255

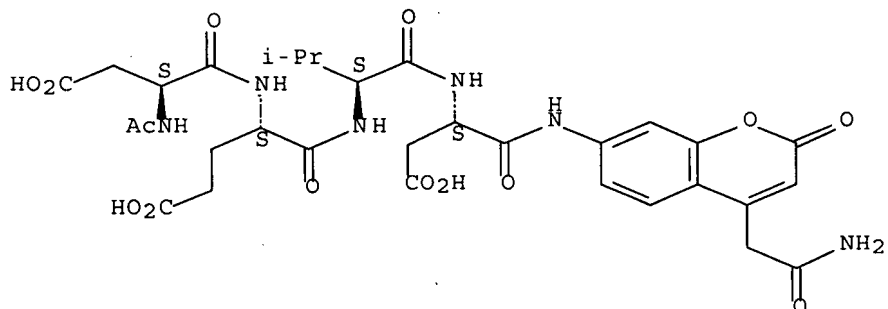
L8 ANSWER 34 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 553676-66-7 REGISTRY

10/686884

ED Entered STN: 24 Jul 2003
CN L- α -Asparagine, N-acetyl-L- α -aspartyl-L- α -glutamyl-L-
valyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI)
(CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C31 H38 N6 O14
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



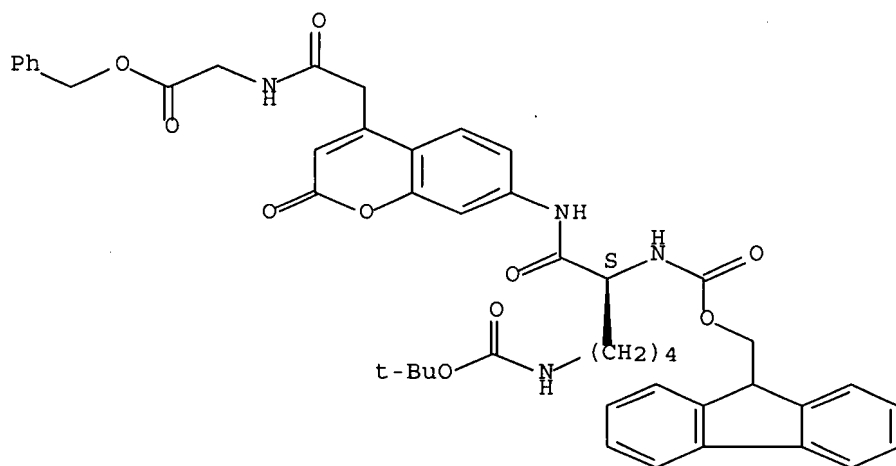
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85629

L8 ANSWER 39 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 525579-02-6 REGISTRY
ED Entered STN: 05 Jun 2003
CN Glycine, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(9H-fluoren-9-
ylmethoxy)carbonyl]-L-lysyl-7-amino-2-oxo-2H-1-benzopyran-4-acetyl-,
phenylmethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C46 H48 N4 O10
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



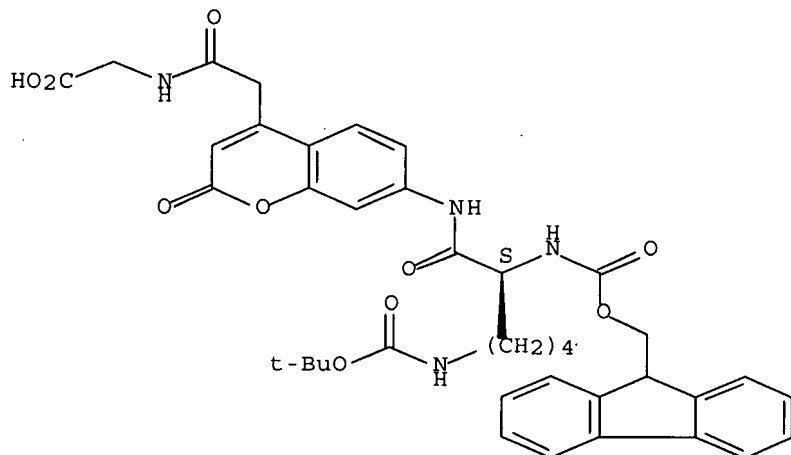
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:381255

L8 ANSWER 41 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 525578-93-2 REGISTRY
ED Entered STN: 05 Jun 2003
CN Glycine, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-7-amino-2-oxo-2H-1-benzopyran-4-acetyl-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H42 N4 O10
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

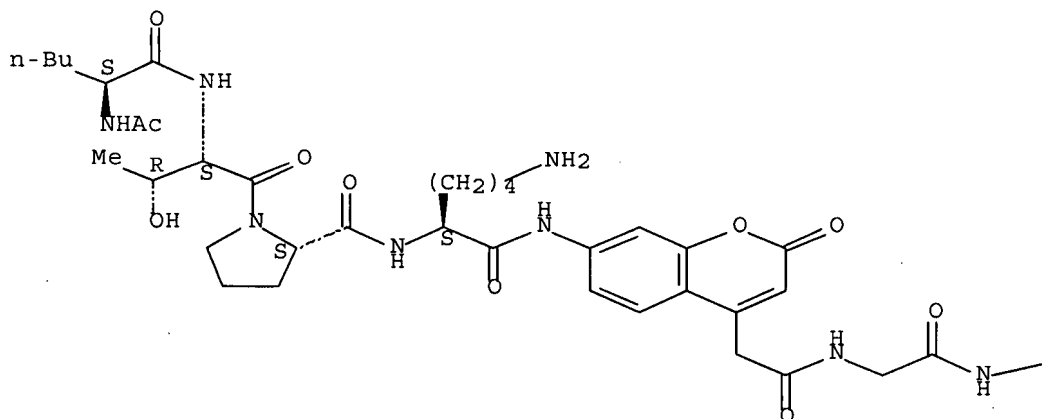
REFERENCE 1: 138:381255

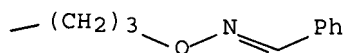
L8 ANSWER 43 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 487011-85-8 REGISTRY
ED Entered STN: 07 Feb 2003
CN Glycinamide, N-acetyl-L-norleucyl-L-threonyl-L-prolyl-L-lysyl-7-amino-
2-oxo-2H-1-benzopyran-4-acetyl-N-[3-[[[(phenylmethylene)amino]oxy]propy
l]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C46 H63 N9 O11
SR CA
LC STN Files: CA, CAPLUS, CASREACT

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry:
Double bond geometry unknown.

PAGE 1-A





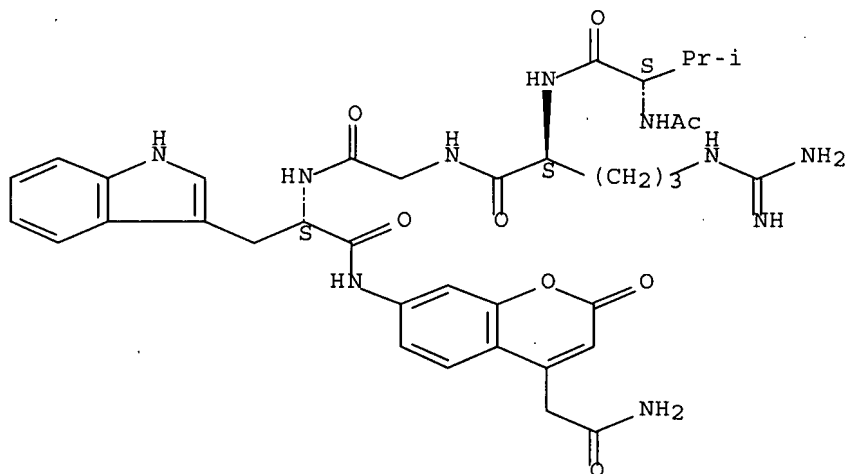
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:102696

L8 ANSWER 71 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 406682-98-2 REGISTRY
ED Entered STN: 23 Apr 2002
CN L-Tryptophanamide, N-acetyl-L-valyl-L-arginylglycyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C37 H46 N10 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



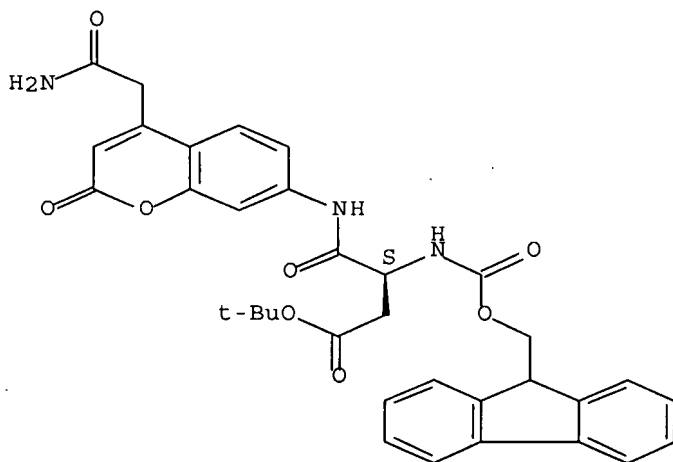
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:275221

L8 ANSWER 78 OF 86 REGISTRY. COPYRIGHT 2007 ACS on STN
RN 403518-96-7 REGISTRY
ED Entered STN: 28 Mar 2002
CN Butanoic acid, 4-[[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]amino]-3-[[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-4-oxo-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H33 N3 O8
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85629

REFERENCE 2: 136:232179

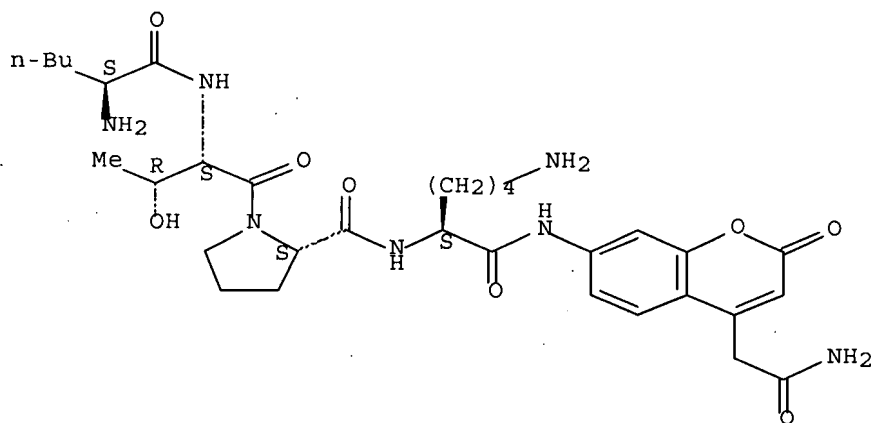
L8 ANSWER 79 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 378247-76-8 REGISTRY
ED Entered STN: 26 Dec 2001
CN L-Lysinamide, L-norleucyl-L-threonyl-L-prolyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H47 N7 O8
SR CA

10/686884

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:20255

L8 ANSWER 80 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN

RN 371979-77-0 REGISTRY

ED Entered STN: 27 Nov 2001

CN L-Argininamide, 1-acetyl-L-prolyl-L-arginyl-L-asparaginyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C34 H49 N13 O9

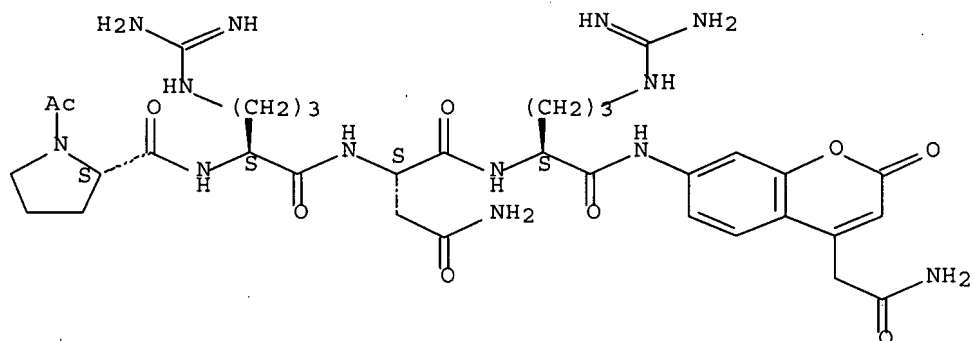
SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

10/686884



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

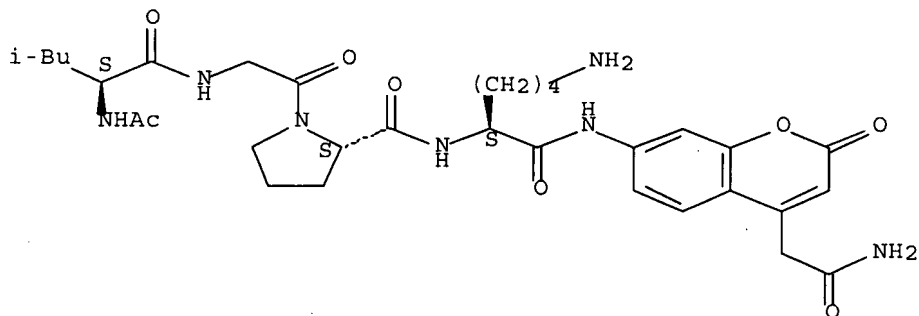
REFERENCE 1: 136:20255

REFERENCE 2: 135:354576

L8 ANSWER 84 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
RN 296236-27-6 REGISTRY
ED Entered STN: 17 Oct 2000
CN L-Lysinamide, N-acetyl-L-leucylglycyl-L-prolyl-N-[4-(2-amino-2-oxoethyl)-2-oxo-2H-1-benzopyran-7-yl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H45 N7 O8
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



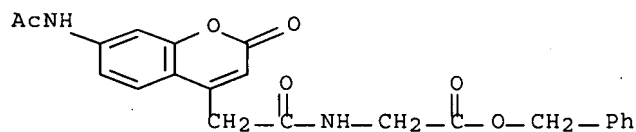
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:20255

REFERENCE 2: 133:248800

L8 ANSWER 86 OF 86 REGISTRY COPYRIGHT 2007 ACS on STN
 RN 141692-68-4 REGISTRY
 ED Entered STN: 05 Jun 1992
 CN Glycine, N-[[7-(acetylamino)-2-oxo-2H-1-benzopyran-4-yl]acetyl]-,
 phenylmethyl ester (9CI) (CA INDEX NAME)
 MF C22 H20 N2 O6
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 117:26258

FILE 'CAOLD' ENTERED AT 10:51:17 ON 08 JUN 2007
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L9 0 L2

FILE 'MEDLINE' ENTERED AT 10:51:33 ON 08 JUN 2007

FILE 'BIOSIS' ENTERED AT 10:51:33 ON 08 JUN 2007
 Copyright (c) 2007 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 10:51:33 ON 08 JUN 2007
 Copyright (c) 2007 Elsevier B.V. All rights reserved.

L10 0 L2

FILE 'CAPLUS' ENTERED AT 10:51:47 ON 08 JUN 2007
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 10:51:47 ON 08 JUN 2007

FILE 'BIOSIS' ENTERED AT 10:51:47 ON 08 JUN 2007
 Copyright (c) 2007 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 10:51:47 ON 08 JUN 2007
 Copyright (c) 2007 Elsevier B.V. All rights reserved.

FILE 'WPIX' ENTERED AT 10:51:47 ON 08 JUN 2007
 COPYRIGHT (C) 2007 THE THOMSON CORPORATION

FILE 'JAPIO' ENTERED AT 10:51:47 ON 08 JUN 2007
 COPYRIGHT (C) 2007 Japanese Patent Office (JPO)- JAPIO

FILE 'PASCAL' ENTERED AT 10:51:47 ON 08 JUN 2007
 Any reproduction or dissemination in part or in full,
 by means of any process and on any support whatsoever
 is prohibited without the prior written agreement of INIST-CNRS.
 COPYRIGHT (C) 2007 INIST-CNRS. All rights reserved.

FILE 'DISSABS' ENTERED AT 10:51:47 ON 08 JUN 2007
 COPYRIGHT (C) 2007 ProQuest Information and Learning Company; All Rights Reserved.

L11 24790 SEA ABB=ON PLU=ON "HARRIS J"?/AU
 L12 159 SEA ABB=ON PLU=ON "BACKES B"?/AU
 L13 724 SEA ABB=ON PLU=ON "ELLMAN J"?/AU
 L14 1108 SEA ABB=ON PLU=ON "CRAIK C"?/AU
 L15 26 SEA ABB=ON PLU=ON L11 AND L12 AND L13 AND L14
 L16 98 SEA ABB=ON PLU=ON L11 AND (L12 OR L13 OR L14)
 L17 42 SEA ABB=ON PLU=ON L12 AND (L13 OR L14)
 L18 43 SEA ABB=ON PLU=ON L13 AND L14
 L19 1117 SEA ABB=ON PLU=ON ((L11 OR L12 OR L13 OR L14 OR L15 OR
 L16 OR L17 OR L18)) AND (PROTEASE OR PROTEINASE)
 L20 150 SEA ABB=ON PLU=ON L19 AND (SUBSTRATE OR PEPTIDE OR
 PROTEIN OR POLYPEPTIDE OR POLYPROTEIN) (5A) LIBRAR?
 L21 18 SEA ABB=ON PLU=ON L20 AND (SS OR SOLID(3A) (PHASE OR
 SUPPORT))
 L22 12 DUP REM L21 (6 DUPLICATES REMOVED)

L22 ANSWER 1 OF 12 MEDLINE on STN
 ACCESSION NUMBER: 2007204394 IN-PROCESS Full-text
 DOCUMENT NUMBER: PubMed ID: 17406604
 TITLE: Substrate activity screening (SAS): a general procedure
 for the preparation and screening of a fragment-based
 non-peptidic protease substrate
 library for inhibitor discovery.
 AUTHOR: Patterson Andrew W; Wood Warren J L; Ellman
 Jonathan A
 CORPORATE SOURCE: Department of Chemistry, University of California,
 Berkeley, CA 94720, USA.
 CONTRACT NUMBER: GM54051 (NIGMS)

10/686884

SOURCE: Nature protocols, (2007) Vol. 2, No. 2, pp. 424-33.
Journal code: 101284307. E-ISSN: 1750-2799.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 5 Apr 2007
Last Updated on STN: 11 Apr 2007

AB Substrate activity screening (SAS) is a fragment-based method for the rapid development of novel substrates and their conversion into non-peptidic inhibitors of Cys and Ser proteases. The method consists of three steps: (i) a library of N-acyl aminocoumarins with diverse, low-molecular-weight N-acyl groups is screened to identify protease substrates using a simple fluorescence-based assay; (ii) the identified N-acyl aminocoumarin substrates are optimized by rapid analog synthesis and evaluation; and (iii) the optimized substrates are converted into inhibitors by direct replacement of the aminocoumarin with known mechanism-based pharmacophores. This protocol describes a general procedure for the solid-phase synthesis of a library of N-acyl aminocoumarin substrates and the screening procedure to identify weak binding substrates.

L22 ANSWER 2 OF 12 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-682655 [70] WPIX
DOC. NO. CPI: C2005-207715 [70]
DOC. NO. NON-CPI: N2005-559952 [70]
TITLE: New phenyl compound useful as probes for a variety of applications e.g. structural elucidation of materials, substrate specificity of enzymes, hybridization of nucleic acids and digestion or degradation of biomolecules
DERWENT CLASS: B04; B05; D16; S01; S03
INVENTOR: BARRIOS A M; CRAIK C S
PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20050207981	A1	20050922	(200570)*	EN	31	[6]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050207981	A1	Provisional	US 2003-519938P 20031114
US 20050207981	A1		US 2004-989590 20041115

PRIORITY APPLN. INFO: US 2004-989590 20041115
US 2003-519938P 20031114

AN 2005-682655 [70] WPIX

AB US 20050207981 A1 UPAB: 20051223

NOVELTY - Phenyl compound (I) (comprises a detectable moiety linked by a covalent bond to a structural moiety, where upon cleavage of the covalent bond, the detectable moiety is capable of forming a complex with a lanthanide ion and the complex imparts a detectable signal) is new.

DETAILED DESCRIPTION - Phenyl compound (I) of formula (R-X-A1-A2-(A-i)_{J-2}) (comprises a detectable moiety linked by a covalent bond to a structural moiety, where upon cleavage of the covalent bond, the detectable moiety is capable of forming a complex with a lanthanide ion and the complex imparts a detectable signal) is new.

R = detectable moiety (optionally substituted by heteroaryl moiety);

A1-A2-(A-i)_{J-2} = structural moiety (an oligomer of amino acid, nucleotide or saccharide residues); X = C(O)-NH, C(O)-O or OP(O)(OH)-O; A1-A-i = an amino acid, a nucleotide or a saccharide residue; J = 1-10 number of residues forming the homo-oligomer such that J-2 is the number of residues in the oligomer sequence exclusive of A1-A2; and

i = position of the residue relevant to A1 and when J is greater than 2, i is the numbers from 3-10. INDEPENDENT CLAIMS are also included for: (1) a library of compounds comprising at least a first and a second members, where each member comprises (I); (2) identifying a substrate specificity of an enzyme comprising contacting members of the library individually with the enzyme at the presence of an lanthanide ion under conditions permissible for the enzyme to cleave the covalent bond linking the detectable moiety and the structural moiety and detecting change in fluorescence or magnetic resonance contrast, where an increase in fluorescence or magnetic resonance contrast indicates cleavage of the covalent bond and determining the substrate specificity of the enzyme from the structural moiety of the member; and (3) detecting the presence of an enzyme in a sample, where the enzyme has a known peptide sequence as the enzyme substrate comprising contacting the sample with (I) at the presence of a lanthanide ion under conditions permissible for the enzyme activity, where (I) comprises the known peptide sequence as the enzyme substrate that and detecting change in fluorescence or magnetic resonance contrast, where the increase in fluorescence or magnetic resonance contrast indicates the presence of the enzyme in the sample.

USE - (I) is useful as a solid supports for the synthesis of individual compounds besides the exemplary detectable moiety-conjugated peptides and libraries consisting of a collection or an array of individual compounds. (I) is also useful as probes for a variety of applications, including structural elucidation of materials, substrate specificity of enzymes, hybridization of nucleic acids, substrate transformation, digestion or degradation of biomolecules (peptides, nucleic acids, saccharides).

L22 ANSWER 3 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 2004:111209 BIOSIS Full-text

DOCUMENT NUMBER: PREV200400114848

TITLE: Profiling of protease specificity using
combinatorial fluorogenic substrate
libraries.

AUTHOR(S): Harris, Jennifer L. [Inventor, Reprint
Author]; Backes, Bradley J. [Inventor];
Ellman, Jonathan A. [Inventor]; Craik,
Charles S. [Inventor]

CORPORATE SOURCE: San Diego, CA, USA

ASSIGNEE: The Regents of the University of California

PATENT INFORMATION: US 6680178 20040120

SOURCE: Official Gazette of the United States Patent and
Trademark Office Patents, (Jan 20 2004) Vol. 1278, No.
3. <http://www.uspto.gov/web/menu/patdata.html>. e-file.
ISSN: 0098-1133 (ISSN print).

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Feb 2004

Last Updated on STN: 25 Feb 2004

AB A method is presented for the preparation and use of fluorogenic peptide substrates that allows for the configuration of general substrate libraries to rapidly identify the primary and extended specificity of enzymes, such as proteases. The substrates contain a fluorogenic-leaving group, such as 7-amino-4-carbamoylmethyl-coumarin (ACC). Substrates incorporating the ACC leaving group show comparable kinetic profiles as those with the traditionally used 7-amino-4-methyl-coumarin (AMC) leaving group. The bifunctional nature of ACC allows for the efficient production of single substrates and substrate libraries using solid-phase synthesis techniques. The approximately 3-fold increased quantum yield of ACC over AMC permits reduction in enzyme and substrate concentrations. As a consequence, a greater number of substrates can be tolerated in a single assay, thus enabling an increase in the diversity space of the library. Soluble positional protease substrate libraries of 137,180 and 6,859 members, possessing amino acid diversity at the P4-P3-P2-P1 and P4-P3-P2 positions, respectively, were constructed. Employing this screening method the substrate specificities of a diverse array of proteases were profiled, including the serine proteases thrombin, plasmin, factor Xa, uPA, tPA, granzyme B, trypsin, chymotrypsin, human neutrophil elastase, and the cysteine proteases papain and cruzain. The resulting profiles create a pharmacophoric portrayal of the proteases allowing for the design of selective substrates and potent inhibitors.

L22 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:707305 CAPLUS Full-text

DOCUMENT NUMBER: 141:380120

TITLE: Synthesis of a PNA-encoded cysteine protease inhibitor library

AUTHOR(S): Debaene, Francois; Mejias, Lorenzo; Harris, Jennifer L.; Winssinger, Nicolas

CORPORATE SOURCE: Institut de Science et Ingenierie Supramoleculaires, Universite Louis Pasteur, Strasbourg, 67000, Fr.

SOURCE: Tetrahedron (2004), 60(39), 8677-8690

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:380120

AB Peptide nucleic acids (PNAs) have been used to encode a combinatorial library whereby each compound is labeled with a PNA tag which reflects its synthetic history and localizes the compound upon hybridization to an oligonucleotide array. We report herein the full synthetic details for a 4000 member fluorescein-labeled PNA-encoded library targeted towards cysteine protease.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:864196 CAPLUS Full-text

DOCUMENT NUMBER: 142:351033

TITLE: PNA-encoded protease substrate microarrays

AUTHOR(S): Winssinger, Nicolas; Damoiseaux, Robert; Tully, David C.; Geierstanger, Bernhard H.; Burdick, Keith; Harris, Jennifer L.

CORPORATE SOURCE: Institut de Science et d'Ingenierie Supramoleculaires, Universite Louis Pasteur, Strasbourg, 67000, Fr.

SOURCE: Chemistry & Biology (2004), 11(10), 1351-1360

CODEN: CBOLE2; ISSN: 1074-5521

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Our current understanding of the role and regulation of protease activity in normal and pathogenic processes is limited by our ability to measure and deconvolute their enzymic activity. To address this limitation, an approach was developed that utilizes rhodamine-based fluorogenic substrates encoded with PNA tags. The PNA tags address each of the substrates to a predefined location on an oligonucleotide microarray through hybridization, thus allowing the deconvolution of multiple signals from a solution. A library of 192 protease substrates was prepared by split and mix combinatorial synthesis. The methodol. and validation of this approach for profiling proteolytic activity from single proteases and from those in crude cell lysates as well as clin. blood samples is described.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:241895 CAPLUS Full-text

DOCUMENT NUMBER: 138:250716

TITLE: Construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination

INVENTOR(S): Backes, Bradley J.; Harris, Jennifer Leslie

PATENT ASSIGNEE(S): IRM, LLC, Bermuda

SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003059847	A1	20030327	US 2002-229950	20020827
WO 2003029823	A1	20030410	WO 2002-US27357	20020827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002331752	A1	20030414	AU 2002-331752	20020827
PRIORITY APPLN. INFO.:			US 2001-315116P	P 20010827
			WO 2002-US27357	W 20020827

AB Non-peptide protease substrate libraries and high purity protease substrate libraries are constructed using fluorogenic compds. Preparation of the fluorogenic protease substrates is described. The libraries are useful in obtaining substrate profiles for a

variety of proteases, such as methods for determining both prime and non-prime protease recognition sequences.

L22 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2003:829805 CAPLUS Full-text
 DOCUMENT NUMBER: 139:381736
 TITLE: Synthesis of a Diverse Library of Mechanism-Based Cysteine Protease Inhibitors
 AUTHOR(S): Wood, Warren J. L.; Huang, Lily; Ellman, Jonathan A.
 CORPORATE SOURCE: Center for New Directions in Organic Synthesis, Department of Chemistry, University of California, Berkeley, CA, 94720, USA
 SOURCE: Journal of Combinatorial Chemistry (2003), 5(6), 869-880
 CODEN: JCCHFF; ISSN: 1520-4766
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 139:381736

AB The authors report improvements for the solid-phase synthesis of mechanism-based mercaptomethyl ketone peptidomimetics as inhibitors of cysteine proteases (Ellman, J. et al., J. Am. Chemical Society 1999, 121, 9907-9914). Specifically, Fmoc-protected chloromethyl ketones were used, rather than the Alloc-protected counterparts. In addition, the authors demonstrated that diverse polar functionalities can be incorporated in the peptidomimetics. Thus, a 2016-membered library of mercaptomethyl ketone was prepared as potential inhibitors. The library was screened against cathepsin B, which is implicated in cancer, resulting in the identification of single-digit nanomolar inhibitors. Because of the diverse functionality incorporated in this library, it should be a rich source of potent inhibitors against many other cysteine proteases.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:946456 CAPLUS Full-text
 DOCUMENT NUMBER: 138:14181
 TITLE: Functional proteomic profiling using combinatorial library
 INVENTOR(S): Winssinger, Nicolas; Harris, Jennifer L.; Backes, Bradley J.; Schultz, Peter G.
 PATENT ASSIGNEE(S): IRM LLC, Bermuda
 SOURCE: PCT Int. Appl., 62 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002099078	A2	20021212	WO 2002-US18065	20020605
WO 2002099078	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

10/686884

NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

AU 2002312389 A1 20021216 AU 2002-312389 20020605
PRIORITY APPLN. INFO.: US 2001-296525P P 20010605
US 2002-363901P P 20020311
WO 2002-US18065 W 20020605

AB Oligonucleotides such as PNA are used to code for the identity of individual members within a library such that a library present as a mixture can be converted into a spatially addressable format through hybridization to an oligonucleotide array. Such a strategy can greatly facilitate arraying small mols., antibodies, proteins and oligosaccharides on a chip and allows for binding or other assays to be performed in solution prior to hybridization. This invention is particularly useful for chemical libraries as it allow for combinatorial synthesis employing split and mix technol. with positional encoding. The decoding is achieved by hybridization to an oligonucleotide. With high d. oligonucleotide arrays, every library member can be analyzed in a highly miniaturized format. As such, this technol. readily lends itself to highly miniaturized screening of single or multiple targets simultaneously and profiling. The present invention provides a novel strategy for encoding the identity of synthesized mols. The methods utilize a stable and easily synthesized PNA tag which is tethered to the small mol. to code for its structure. In one embodiment, the present invention provides a method for identifying a compound that binds a protein, the method comprising: providing a library of compds., wherein each of the compds. comprises a peptide nucleic acid identifier tag; hybridizing the library of compds. to an array of oligonucleotides; contacting the array of bound compds. with a protein; and detecting the compds. that bind the target.

L22 ANSWER 9 OF 12 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002163544 EMBASE Full-text
TITLE: Combinatorial strategies for targeting protein families: Application to the proteases.
AUTHOR: Maly D.J.; Huang L.; Ellman J.A.
CORPORATE SOURCE: Prof. J.A. Ellman, Department of Chemistry, University of California, Berkeley, CA 94720-1460, United States. jellman@uclink.berkeley.edu
SOURCE: ChemBioChem, (4 Jan 2002) Vol. 3, No. 1, pp. 17-37. .
Refs: 93
ISSN: 1439-4227 CODEN: CBCHFX
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002

AB Tens of thousands of proteins have been identified as a result of recent large scale genomic and proteomic efforts. With this large influx of new proteins, the formidable task of elucidating their function begins. However, this task becomes more manageable if proteins are divided into families based upon sequence homology, thereby allowing tools for their systematic study to be

developed based upon their common structural and mechanistic characteristics, Combinatorial chemistry is ideally suited for the systematic study of protein families because a large amount of diversity can be readily displayed about a common scaffold designed to target a given protein family. Targeted combinatorial libraries have been particularly effective for the study of a ubiquitous family of proteins, the proteases. Substrate-specificity profiles of many proteases have been determined by using combinatorial libraries of appropriately labeled peptides. This specificity information has been utilized to identify the physiological protein substrates of these enzymes and has facilitated inhibitor design efforts. Furthermore, combinatorial libraries of small molecules prepared with mechanism-based scaffolds have resulted in the identification of potent, small-molecule inhibitors of numerous proteases. Cell-permeable small-molecule inhibitors identified by these methods have served as powerful chemical tools to study protease function in vitro and in vivo and have served as leads for the development of therapeutic agents.

L22 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2001:904143 CAPLUS Full-text

DOCUMENT NUMBER: 136:20255

TITLE: Profiling of protease specificity using
combinatorial fluorogenic substrate
libraries

INVENTOR(S): Harris, Jennifer L.; Backes,
Bradley J.; Ellman, Jonathan A.;
Craik, Charles S.

PATENT ASSIGNEE(S): Regents of the University of California, USA

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

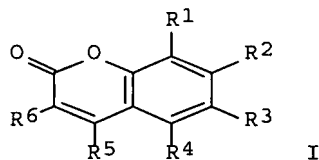
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094332	A1	20011213	WO 2001-US17265	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002022243	A1	20020221	US 2001-866132	20010525
US 6680178	B2	20040120		
US 2004175777	A1	20040909	US 2003-686884	20031015
PRIORITY APPLN. INFO.:			US 2000-209274P	P 20000602
			US 2001-866132	A 20010525
			WO 2001-US17265	A 20010525

OTHER SOURCE(S): MARPAT 136:20255

GI



AB Fluorogenic peptide substrates allow for the configuration of general substrate libraries to rapidly identify the primary and extended specificity of enzymes, such as proteases. Coumarin derivs. I [R1-R6 are H, halo, NO₂, CN, C(O)mR7, C(O)NR8R9, S(O)tR10, SO₂NR11R12, OR13, (un)substituted alkyl, -R14-SS or NHR15, where R7-R13 are H, (un)substituted alkyl or aryl; R14 is a linking group adjoining the fluorogenic moiety and the solid support (SS); R15 is an amine-protecting group, -C(O)-AA or -C(O)-P, where P is a peptide sequence and AA is an amino acid residue; m = 1 or 2; t = 0-2, with the proviso that at least one of R1-R6 is -R14-SS and at least one of R1-R6 is NHR15] are claimed. The substrates contain a fluorogenic-leaving group, such as 7-amino-4-carbamoylmethylcoumarin (ACC). Substrates incorporating the ACC leaving group show comparable kinetic profiles as those with the traditionally used 7-amino-4-methylcoumarin (AMC) leaving group. The bifunctional nature of ACC allows for the efficient production of single substrates and substrate libraries using solid-phase synthesis techniques. The approx. 3-fold increased quantum yield of ACC over AMC permits reduction in enzyme and substrate concns., so that a greater number of substrates can be tolerated in a single assay, thus enabling an increase in the diversity space of the library. Employing this screening method, the substrate specificities of a diverse array of proteases were profiled, including serine proteases and cysteine proteases.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2000:494458 CAPLUS Full-text

DOCUMENT NUMBER: 133:248800

TITLE: Rapid and general profiling of protease specificity by using combinatorial fluorogenic substrate libraries

AUTHOR(S): Harris, Jennifer L.; Backes, Bradley J.; Leonetti, Francesco; Mahrus, Sami; Ellman, Jonathan A.; Craik, Charles S.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Program in Chemistry and Chemical Biology, University of California, San Francisco, CA, 94143, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(14), 7754-7759

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method is presented for the preparation and use of fluorogenic peptide substrates that allows for the configuration of general substrate libraries to

rapidly identify the primary and extended specificity of proteases. The substrates contain the fluorogenic leaving group 7-amino-4-carbamoylmethylcoumarin (ACC). Substrates incorporating the ACC leaving group show kinetic profiles comparable to those with the traditionally used 7-amino-4-methylcoumarin (AMC) leaving group. The bifunctional nature of ACC allows for the efficient production of single substrates and substrate libraries by using 9-fluorenylmethoxycarbonyl (Fmoc)-based solid-phase synthesis techniques. The approx. 3-fold-increased quantum yield of ACC over AMC permits reduction in enzyme and substrate concns. As a consequence, a greater number of substrates can be tolerated in a single assay, thus enabling an increase in the diversity space of the library. Soluble positional protease substrate libraries of 137,180 and 6859 members, possessing amino acid diversity at the P4-P3-P2-P1 and P4-P3-P2 positions, resp., were constructed. Employing this screening method, we profiled the substrate specificities of a diverse array of proteases, including the serine proteases thrombin, plasmin, factor Xa, urokinase-type plasminogen activator, tissue plasminogen activator, granzyme B, trypsin, chymotrypsin, human neutrophil elastase, and the cysteine proteases papain and cruzain. The resulting profiles create a pharmacophoric portrayal of the proteases to aid in the design of selective substrates and potent inhibitors.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:107634 CAPLUS Full-text

DOCUMENT NUMBER: 132:262012

TITLE: Synthesis of positional-scanning libraries of fluorogenic peptide

substrates to define the extended substrate specificity of plasmin and thrombin

AUTHOR(S): Backes, Bradley J.; Harris, Jennifer L.; Leonetti, Francesco; Craik, Charles S.; Ellman, Jonathan A.

CORPORATE SOURCE: Chemistry Department, University of California Berkeley, Berkeley, CA, 94720, USA

SOURCE: Nature Biotechnology (2000), 18(2), 187-193
CODEN: NABIF9; ISSN: 1087-0156

PUBLISHER: Nature America

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have developed a strategy for the synthesis of positional-scanning synthetic combinatorial libraries (PS-SCL) that does not depend on the identity of the P1 substituent. To demonstrate the strategy, we synthesized a tetrapeptide positional library in which the P1 amino acid is held constant as a lysine and the P4-P3-P2 positions are positionally randomized. The 6859 members of the library were synthesized on solid support with an alkane sulfonamide linker, and then displaced from the solid support by condensation with a fluorogenic 7-amino-4-methylcoumarin-derivatized lysine. This library was used to determine the extended substrate specificities of two trypsin-like enzymes, plasmin and thrombin, which are involved in the blood coagulation pathway. The optimal P4 to P2 substrate specificity for plasmin was P4-Lys/Nle (norleucine)/Val/Ile/Phe, P3-Xaa, and P2-Tyr/Phe/Trp. This cleavage sequence has recently been identified in some of plasmin's physiol. substrates. The optimal P4 to P2 extended substrate sequence determined for thrombin was P4-Nle/Leu/Ile/Phe/Val, P3-Xaa, and P2-Pro, a sequence found in many of the physiol. substrates of thrombin. Single-substrate kinetic anal. of plasmin and thrombin was used to validate the substrate preferences resulting from the PS-SCL. By three-dimensional structural modeling of the substrates into the active sites of plasmin and thrombin, we identified potential

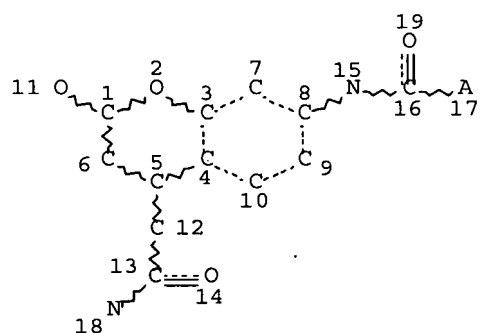
10/686884

determinants of the defined substrate specificity. This method is amenable to the incorporation of diverse substituents at the P1 position for exploring mol. recognition elements in proteolytic enzymes.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

FILE 'HOME' ENTERED AT 10:57:09 ON 08 JUN 2007

L1 STR



NODE ATTRIBUTES:

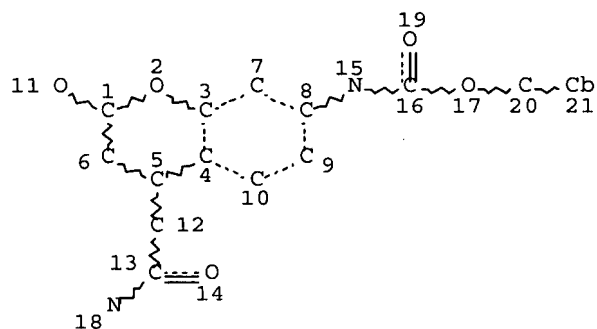
NSPEC IS RC AT 17
 CONNECT IS X2 RC AT 6
 CONNECT IS X2 RC AT 7
 CONNECT IS X2 RC AT 9
 CONNECT IS X2 RC AT 10
 CONNECT IS X2 RC AT 12
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 116 SEA FILE=REGISTRY.SSS FUL L1
 L3 STR



NODE ATTRIBUTES:

CONNECT IS X2 RC AT 6
 CONNECT IS X2 RC AT 7
 CONNECT IS X2 RC AT 9
 CONNECT IS X2 RC AT 10
 CONNECT IS X2 RC AT 12
 DEFAULT MLEVEL IS ATOM
 GGCAT IS PCY AT 21
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

10/686884

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L4 1 SEA FILE=REGISTRY SUB=L2 SSS FUL L3

FILE 'REGISTRY' ENTERED AT 10:36:47 ON 08 JUN 2007
ACT HAJ1/A

L1 STR
L2 116 SEA SSS FUL L1

FILE 'REGISTRY' ENTERED AT 10:38:11 ON 08 JUN 2007
D QUE STAT

L3 STR L1
L4 1 SEA SUB=L2 SSS FUL L3
D QUE STAT

FILE 'CAPLUS' ENTERED AT 10:45:21 ON 08 JUN 2007
L5 1 SEA ABB=ON PLU=ON L4
D IBIB ABS HITSTR

FILE 'REGISTRY' ENTERED AT 10:45:45 ON 08 JUN 2007
D QUE
D QUE STAT
D QUE STAT L2

FILE 'CAPLUS' ENTERED AT 10:46:29 ON 08 JUN 2007
L6 15 SEA ABB=ON PLU=ON L2
L7 14 SEA ABB=ON PLU=ON L6 NOT L5
SEL HIT L7 1-14 RN
D 1-14

FILE 'REGISTRY' ENTERED AT 10:48:21 ON 08 JUN 2007
L8 86 SEA ABB=ON PLU=ON (296236-25-4/BI OR 296236-27-6/BI OR
371979-74-7/BI OR 371979-75-8/BI OR 371979-76-9/BI OR
371979-77-0/BI OR 525578-92-1/BI OR 525579-01-5/BI OR
141692-68-4/BI OR 378247-76-8/BI OR 403518-96-7/BI OR
406682-92-6/BI OR 406682-93-7/BI OR 406682-94-8/BI OR
406682-95-9/BI OR 406682-96-0/BI OR 406682-97-1/BI OR
406682-98-2/BI OR 487011-47-2/BI OR 487011-48-3/BI OR
487011-49-4/BI OR 487011-50-7/BI OR 487011-62-1/BI OR
487011-63-2/BI OR 487011-64-3/BI OR 487011-65-4/BI OR
487011-66-5/BI OR 487011-67-6/BI OR 487011-68-7/BI OR
487011-69-8/BI OR 487011-70-1/BI OR 487011-71-2/BI OR
487011-72-3/BI OR 487011-73-4/BI OR 487011-74-5/BI OR
487011-75-6/BI OR 487011-76-7/BI OR 487011-77-8/BI OR
487011-78-9/BI OR 487011-79-0/BI OR 487011-80-3/BI OR
487011-81-4/BI OR 487011-82-5/BI OR 487011-83-6/BI OR
487011-84-7/BI OR 487011-85-8/BI OR 525578-93-2/BI OR
525579-02-6/BI OR 553676-58-7/BI OR 553676-59-8/BI OR
553676-62-3/BI OR 553676-64-5/BI OR 553676-66-7/BI OR
608529-60-8/BI OR 608529-68-6/BI OR 847549-05-7/BI OR
847549-06-8/BI OR 847549-07-9/BI OR 847549-08-0/BI OR
862896-00-2/BI OR 863975-27-3/BI OR 884005-67-8/BI OR
884005-68-9/BI OR 884005-69-0/BI OR 884005-70-3/BI OR
884005-71-4/BI OR 884005-74-7/BI OR 884005-75-8/BI OR
884005-76-9/BI OR 884005-77-0/BI OR 884005-78-1/BI OR
884005-79-2/BI OR 890405-98-8/BI OR 890405-99-9/BI OR

10/686884

890406-00-5/BI OR 890406-01-6/BI OR 890406-02-7/BI OR
890406-03-8/BI OR 890406-04-9/BI OR 890406-05-0/BI OR
890406-06-1/BI OR 912840-50-7/BI OR 912840-52-9/BI OR
912840-53-0/BI OR 912840-63-2/BI OR 912840-65-4/BI)

D QUE

D 1-86 REG

D 1,6,13,26-28,32,34,39,41,43,71,78-80,84,86 IDE CAN

FILE 'CAOLD' ENTERED AT 10:51:17 ON 08 JUN 2007

L9 0 SEA ABB=ON PLU=ON L2

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:51:33 ON 08 JUN 2007

L10 0 SEA ABB=ON PLU=ON L2

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS'
ENTERED AT 10:51:47 ON 08 JUN 2007

L11 24790 SEA ABB=ON PLU=ON "HARRIS J"?/AU
L12 159 SEA ABB=ON PLU=ON "BACKES B"?/AU
L13 724 SEA ABB=ON PLU=ON "ELLMAN J"?/AU
L14 1108 SEA ABB=ON PLU=ON "CRAIK C"?/AU
L15 26 SEA ABB=ON PLU=ON L11 AND L12 AND L13 AND L14
L16 98 SEA ABB=ON PLU=ON L11 AND (L12 OR L13 OR L14)
L17 42 SEA ABB=ON PLU=ON L12 AND (L13 OR L14)
L18 43 SEA ABB=ON PLU=ON L13 AND L14
L19 1117 SEA ABB=ON PLU=ON ((L11 OR L12 OR L13 OR L14 OR L15 OR
L16 OR L17 OR L18)) AND (PROTEASE OR PROTEINASE)
L20 150 SEA ABB=ON PLU=ON L19 AND (SUBSTRATE OR PEPTIDE OR
PROTEIN OR POLYPEPTIDE OR POLYPROTEIN) (5A) LIBRAR?
L21 18 SEA ABB=ON PLU=ON L20 AND (SS OR SOLID(3A) (PHASE OR
SUPPORT))
L22 12 DUP REM L21 (6 DUPLICATES REMOVED)
D 1-12 IBIB ABS

FILE 'HOME' ENTERED AT 10:57:09 ON 08 JUN 2007

D QUE L4

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 7 JUN 2007 HIGHEST RN 936802-99-2

DICTIONARY FILE UPDATES: 7 JUN 2007 HIGHEST RN 936802-99-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

FILE CAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 8 Jun 2007 VOL 146 ISS 25
FILE LAST UPDATED: 7 Jun 2007 (20070607/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 8 Jun 2007 VOL 146 ISS 25
FILE LAST UPDATED: 7 Jun 2007 (20070607/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CAOLD

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

FILE MEDLINE

FILE LAST UPDATED: 7 Jun 2007 (20070607/UP). FILE COVERS 1950 TO DAT

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 6 June 2007 (20070606/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE

FILE COVERS 1974 TO 7 Jun 2007 (20070607/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIX

FILE LAST UPDATED:

29 MAY 2007 <20070529/UP>

MOST RECENT THOMSON SCIENTIFIC UPDATE: 200734 <200734/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> New reloaded DWPI Learn File (LWPI) available as well <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> New display format FRAGHITSTR available <<<

SEE ONLINE NEWS and

[http://www.stn-international.de/archive/stn_online_news/fraghitstr ex.](http://www.stn-international.de/archive/stn_online_news/fraghitstr_ex)

>>> IPC Reform backfile reclassification has been loaded to 31 Decembe
2006. No update date (UP) has been created for the reclassified
documents, but they can be identified by 20060101/UPIC and
20061231/UPIC. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE

http://www.stn-international.de/stndatabases/details/ipc_reform.html a

<http://scientific.thomson.com/media/scpdf/ipcrdwpf.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE

http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FILE JAPIO

FILE LAST UPDATED: 27 APR 2007 <20070427/UP>

FILE COVERS APRIL 1973 TO JANUARY 25, 2007

>>> GRAPHIC IMAGES AVAILABLE <<<

10/686884

FILE PASCAL

FILE LAST UPDATED: 4 JUN 2007 <20070604/UP>

FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

FILE DISSABS

FILE COVERS 1861 TO 25 MAY 2007 (20070525/ED)

Only fair use as provided by the United States copyright law is permitted. PROQUEST INFORMATION AND LEARNING COMPANY MAKES NO WARRANTY REGARDING THE ACCURACY, COMPLETENESS OR TIMELINESS OF THE LICENSED MATERIALS OR ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, AND SHALL NOT BE LIABLE FOR DAMAGES OF ANY KIND OR LOST PROFITS OR OTHER CLAIMS RELATED TO THE LICENSED MATERIALS OR THEIR USE.

FILE HOME